



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/740,393 | 12/18/2000 | Manfred Weigele | 395D US | 3200 |

7590

03/06/2003

David L. Bernstein
ARIAD Pharmaceuticals, Inc.
26 Landsdowne Street
Cambridge, MA 02139-4234

EXAMINER

BERCH, MARK L

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 03/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/740,393

Applicant(s)

WEIGELE ET AL.

Examiner

Mark L. Berch

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Art Unit: 1624

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 10-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Charubala.

Compounds 5, 6, 9, 14 anticipate. In claim 1, proviso (A) is met by either branch, Proviso (B) does not apply because its condition is not met and proviso (C) is met by branch (1). In addition, 29, 30, 32 and 33 anticipate because proviso (C) is met by branch (3). The cyano-alkoxy is not a prohibited value for R^J.

Claims 1-3, 10-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Brush et al.

See the structure formed in figure 1B; proviso (C) is met by branch (1) and (3) both.

Claims 1-3, 10-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Tate.

Compounds 1 and 9 in figure 1 anticipate. In claim 1, proviso (A) is met by either branch, Proviso (B) does not apply because its condition is not met and proviso (C) is met by branch (1) and by branch (3), since the heteroaliphatic-oxy is not a prohibited value for R^J.

Claims 1-3, 6-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wada.

In scheme 2, see 7a, 10b, 10c, 9a, 13b, which anticipate claims 6-9, as these claims have no relevant provisos. In addition, 7a, 8a and 9a anticipate claims 1-3, 10-15, 18 because proviso (C) is met by branch (3). The cyano-ethoxy (CE) is not a prohibited value for R^J.

Claims 1-3, 10-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Filippov.

For 2, 5 and 6, proviso (C) is met by branch (3). The cyano-ethoxy (OCE) and the cycloalkyloxy are both not a prohibited value for R^J. Moreover, for (1) and (2) branch (1) of C is also met. For Proviso (B), the condition is met for 2, 5 and 6, even if a very broad definition of "derivative" is used (see point 10 below), because, although there is a heteroatom attached to the cycloalkyl ring, there is no halogen. Compound (1) satisfies the proviso because its R^B is none of those choices.

Claims 1-3, 6-15, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Kondo.

See compound 4b, which because of the sulfur meets branch (3) of proviso C) and because of the S anticipates claims such as 6.

The traverse is unpersuasive. Applicants are reading into the claims a limitation which is not present. Applicants state that the P-containing moiety "is a substituent on an aliphatic....moiety which is attached to the nitrogen." But the claims do not state anything nearly that narrow. The claim language is simply that it is an aliphatic, etc moiety which comprises P. It does not forbid the moiety from being attached via the P.

Art Unit: 1624

In each case, the moiety has both the Phosphorous piece and the aliphatic, etc piece, and that is all the claims require.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-46 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-174 of copending Application No. 09/740653. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the two cases are broadly overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1624

Claim 1-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. It is unknown what "terminating in a cyano" at page 99, line 24 requires. Cyano is self terminating, as it can take no further substituent. Thus, would CH(CN)Ethyl be terminated with CN, and the ethyl is just a substituent on the cyano-methyl? Or is it not terminated, as the ethyl continues the chain? The traverse is unpersuasive. Applicants have not addressed the issue or the question stated. The statement "Terminating in a cyano group means having a terminal cyano." Is just a tautology; it does not address the question. It is not clear in CH(CN)Ethyl whether the cyano is "terminal" or not.
2. Which amino acid ---any molecule containing an amino group and an acid function? Would the language include carbamic acid, or aminobenzenesulfonic acid? (6th from last line of claim 1).
3. In claim 2, 7th from last line, Y links R1 and either carbonyl or sulfonyl. But claim 2, line 6 refers to linking it to P. Does this means that at seventh from last line of claim 2, last two choices, it cannot be a bond? Applicants respond that, so long as R1 is not H, that Y can be a bond, but that contradicts the text at claim 2, line 6, which mentions it linking to P, but not to the sulfonyl or the carbonyl.
4. Fourth from last line of claim 2 mentions a variable M' but does not define it. The traverse is unpersuasive. There is no such "convention" set forth in the claim. M and M-prime are not the same thing.

Art Unit: 1624

5. Page 100, lines 33-34 is unclear. How could a methylene group be unsaturated? By its very nature, methylene is saturated. The traverse is unpersuasive. The explanation is unconnected to the actual claim language. The claim does not say "2-carbon unit". It says that M is optionally substituted methylene, which is optionally substituted CH_2 . It does not say that M is simply a carbon. Two of the connected together would be optionally substituted $(\text{CH}_2)_2$, which is not unsaturated.
6. The term "or a pharmaceutically acceptable derivative thereof" (e.g. claim 1, line 1) is of unknown scope. What is a derivative? What level of change can be made in the compounds and it still be a derivative? Can the P be removed? The traverse is unpersuasive. Applicants point to page 30, lines 16 - page 31, line 26. However, that just covers the salt, the ester and the prodrug. The term "derivative" is not limited to those three.
7. No independent definition is given for R^k . For whatever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice was intended. This is the same issue as point 4.
8. The term "acyl" (e.g. page 102, line 13) is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. $\text{RC}(\text{O})$, what is R? The traverse is unpersuasive. Applicants refer to "the context of the document" but it is unclear what that refers to.
9. Claim 5, second from last line of page 4, has "sulfate, sulfonate, sulfate, sulfonate," which is duplicative. This occurs in other places where the variable R_3 occurs.
10. In claim 5, Sulfonate makes no sense. It is a divalent radical but is used for a monovalent moiety. Likewise "sulfate" is divalent. Likewise in claim 36. The traverse

Art Unit: 1624

is unpersuasive. Applicants have misdrawn these groups. Sulfonate is $-S(O)_2O-$, divalent, and sulfate is $-OS(O)_2O-$. The $-SO_3H$ group is the sulfo group, and the $-OSO_2H$ group is the bisulfite group.

11. The intended scope of "Phosphorous containing moieties" is unclear. Could this include a cationic substituent which had a phosphate anion as a counterion, or an anionic substituent (e.g. carboxylate) with a phosphonium cation as a counterion? Would it include P atoms without functional groups, such as $-PO_2$ or phosphazene rings? Would it include highly reactive groups such as $-PCl_2$? The traverse is unpersuasive. The page 25 discussion is completely open-ended and does not discuss these issues. Applicants statement that the term "is defined on page 25, lines 25-31" is not accurate. It simply gives examples of moieties which the term "includes but is not limited to". Thus, the above questions remain unanswered.
12. Claims 36-38 lack definitions for Y and R1.
13. Because of the first comma at page 114, line 5, it is unclear whether R3 is a choice for R^A or just a substituent on the aryl.
14. Claim 39 lacks a definition for R6.
15. Claim 17 has ZR for the last choice for R^C . However, R is not defined when used in R^C . Elsewhere in the claim are 2 definitions for R, one within the definition of Z and one within the definition of R^D so it is unclear which, if any, of these is intended. Note that these definitions are different Likewise claim 37-39. The traverse is unpersuasive. There are two definitions; the claim does not indicate which one to use. Applicants point to "each occurrence of R without a further alpha numeric

Art Unit: 1624

subscript.” That just make it clear that one is providing a definition for R, and not for e.g. R^A .

16. Claim 36 has the same problem. The variable R appears within the definition of R^C , Z, R^D and R^3 .

17. The claim 36 definition of R^3 is now garbled. The list starts after the structures at the top of page 27 and runs for three lines, and then starts all over again with a very similar list.

Claims 43 and 46 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

There is no way of knowing what this is supposed to cover. There are vast numbers of kinases. The largest area is protein kinases. One major classification scheme for these is as follows:

1.AGC Group

1.AGC Group I Cyclic nucleotide regulated protein kinase (PKA & PKG) family

2.AGC Group II Diacylglycerol-activated/phospholipid-dependent protein kinase C (PKC) family

3.AGC Group III Related to PKA and PKC (RAC/Akt) protein kinase family

4.AGC Group IV Kinases that phosphorylate G protein-coupled receptors family

5.AGC Group V Budding yeast AGC-related protein kinase family

6.AGC group VI Kinases that phosphorylate ribosomal protein S6 family

7.AGC Group VII Budding yeast DBF2/20 family

8.AGC Group VIII Flowering plant PVPK1 protein kinase homolog family

Art Unit: 1624

9.AGC Group Other Other AGC related kinase families

2.CaMK Group

1.CaMK Group I Kinases regulated by Ca^{2+} /CaM and close relatives family

2.CaMK Group II KIN1/SNF1/Nim1 family

3.CaMK Other Other CaMK related kinase families

3.CMGC Group

1.CMGC Group I Cyclin-dependent kinases (CDKs) & close relatives family

2.CMGC Group II ERK (MAP) kinase family

3.CMGC Group III Glycogen synthase kinase 3 (GSK3) family

4.CMGC Group IV Casein kinase II family

5.CMGC Group V Clk family

6.CMGC Group Other

4.PTK Group - 'Conventional' protein-tyrosine kinases

1.PTK group I Src family

2.PTK Group II Tec/Atk family

3.PTK Group III Csk family

4.PTK Group IV Fes (Fps) family

5.PTK Group V Abl family

6.PTK Group VI Syk/ZAP70 family

7.PTK Group VII Tyk2/Jak1 family

8.PTK Group VIII Ack family

9.PTK Group IX Focal adhesion kinase (Fak) family

10.PTK Group X Epidermal growth factor receptor family

Art Unit: 1624

- 11.PTK Group XI Eph/Elk/Eck receptor family
- 12.PTK Group XII Axl family
- 13.PTK Group XIII Tie/Tek family
- 14.PTK Group XIV Platelet-derived growth factor receptor family
- 15.PTK Group XV Fibroblast growth factor receptor family
- 16.PTK Group XVI Insulin receptor family
- 17.PTK Group XVII LTK/ALK family
- 18.PTK Group XVIII Ros/Sevenless family
- 19.PTK Group XIX Trk/Ror family
- 20.PTK Group XX DDR/TKT family
- 21.PTK Group XXI Hepatocyte growth factor receptor family
- 22.PTK Group XXII Nematode Kin15/16 family
- 23.PTK Other membrane spanning kinases Other PTK kinase families

5.OPK Group - Other protein kinases (not falling in major groups)

- 1.OPK Group I Polo family
- 2.OPK Group II MEK/STE7 family
- 3.OPK Group III PAK/STE20 family
- 4.OPK Group IV MEKK/STE11 family
- 5.OPK Group V NimA family
- 6.OPK Group VI weel/mik1 family
- 7.OPK Group VII Kinases involved in transcriptional control family
- 8.OPK Group VIII Raf family
- 9.OPK Group IX Activin/TGFb receptor family

Art Unit: 1624

10.OPK Group X Flowering plant putative receptor kinases and close relatives family

11.OPK Group XI PSK/PTK "mixed lineage" leucine zipper domain family

12.OPK Group XII Casein kinase I family

13.OPK Group XIII PKN prokaryotic protein kinase family

14.OPK Other Other protein kinase families (each with no close relatives)

Further, each of these subgroups has many members. Just as an example CaMK Group I has CaMKIIa; CaMKIIb; CaMKIIg; CaMKIId; DmCamKII; CamKI; CaMKIV; DdMLCK; DUN1; PSK-H1 ; CMKI; CMK2; ACMPK; MLCK-K; MLCK-M; Titen; TWITCH; MRE4; PhKgM; PhKgT; RSK1C; RSK2C; ASK1; ASK2; CDPK; AK1; OsSPK, and there may be more as well.

Moreover, members of a groups can be substantially different. For example, The pattern of expression of JAK3 contrasts sharply even with that of other Janus kinases (JAK1, JAK2, and TYK2), which are ubiquitously expressed, as opposed to JAK3 whose expression appears to be limited to certain cells. In addition, even a single kinase can exist in numerous variants.

And this is just one category of kinases. In addition to protein kinases, there are many others, including Adenylylsulfate kinases, Guanylate kinases, Diacylglycerol kinases, GHMP kinases, Deoxynucleoside kinases, gluconokinases (gluconate kinases), Adenylatekinases, 6-Phosphofructo-2-kinases, Nucleoside diphosphate kinases, Choline/ethanolamine kinases, Carbohydrate kinases (for which there are a number of families, each with numerous members), Phosphofructokinases, Riboflavin kinases, Prokaryotic diacylglycerol kinases, glycerol kinases, xylulokinases,

ribulokinases, rhamnulokinases, fucokinases, Hexokinases and others. There are thousands of kinases, with new ones being discovered every month. They are extremely diverse in their distribution, expression, regulation, form, function, etc.

Claims 43, 45 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enable for tumors generally, including cancer, is not present, for claims 43 and 45. Enablement for the unknown diseases covered by claims 43 and 46 for the "kinase" (see above) is also not present.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims.

(a) Scope of the compounds. Because of the extremely broad nature of the 4 substituents on the purine nucleus, trillions of compounds are embraced.

(b) Scope of the diseases covered. A) Tumors. The coverage is immense. There are hundreds of types of cancers and tumors. They can occur in pretty much every part of the body. Further, such a term also covers precancerous conditions such as lumps, lesions, and polyps. In addition, "tumor" covers things other than neoplasms. It also covers any kind of swelling arising from inflammation. Thus, the claim would cover treatment of many kinds of inflammation. B) Kinase diseases. The scope is simply not known. It is unclear which kinases are being referred to, and even of those, it is not known which diseases are mediated by these kinases.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information is totally generic with regard to the disorder. Thus, the same dosage is given for whatever hundreds of diseases are covered. A) For cancers, a number of broad categories are given such as lymphomas, lung cancers and leukemias, along with a list of smaller categories and individual cancers. individual cancers. There are dozens of leukemias. There are B-Cell Neoplasms such as B-cell prolymphocytic leukemia and Hairy cell leukemia. There are T-Cell Neoplasms such as T-cell prolymphocytic leukemia, aggressive NK cell leukemia, and T-cell granular lymphocytic leukemia. There are different kinds of acute myeloid leukemias, acute promyelocytic leukemias, acute myelomonocytic leukemia, chronic myelomonocytic leukemia, acute monocytic

leukemias, and erythroleukemias. There is also acute megakaryoblastic leukemia, acute promyelocytic leukemia, Multiple Myeloma, lymphoblastic leukemia, hypocellular acute myeloid leukemia, Ph-/BCR- myeloid leukemia, acute basophilic leukemia, acute myelofibrosis, chronic granulocytic leukemia, chronic neutrophilic leukemia, chronic eosinophilic leukemia and many others. No compound has ever been found effective generally against leukemias because they are simply too diverse. B) For kinases, only one is named, src on page 32. But the claim covers any kinase that any of these trillions of compounds might be effective against.

(4) State of the Prior Art: A). The prior art knows that there never has been a compound capable of treating cancer generally. There are compounds that treat a modest range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. B). For reasons set forth above in the indefiniteness rejection, the prior art is even less clear here, because even what diseases are involved is unclear.

(5) Working Examples: There are none. Example 48 contains an assortment of various cell tests. However, no specific data is presented for any particular compound. And

Art Unit: 1624

since these are just basic cell tests, even if data were presented on particular compounds, these are not examples of treatment.

(6) Skill of those in the art: A). It is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task. The skill thus depends on the particular cancer involved. There are cancers where the skill level is high and there are multiple successful chemotherapeutic treatments. In many, many cancers, however, there is no chemotherapy whatsoever available. The majority of common cancers do not respond to chemotherapy. B). The science of using inhibitors of kinases to treat disease is very much in its infancy. Moreover, the specific function of most of these kinases is unknown. The notion of using kinase inhibitors to prevent disease is presently beyond what medical science can accomplish.

(7) The quantity of experimentation needed: Given the fact that historically the development of new cancers drugs has been difficult and time consuming, and especially in view of factors 1, 6 and 4, the quantity of experimentation needed is expected to be great. For kinases, it would be overwhelming, since most kinases, there is almost nothing, or nothing, known about their disease involvement.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.



Mark L. Berch
Primary Examiner
Art Unit 1624

March 3, 2003